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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,763	05/12/2005	Heinz Peter Vollmers	50308/003001	8912

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EXAMINER	
HALVORSON, MARK	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,763	VOLLMERS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/8/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4, 7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 4, 7-16 are pending, and examined on the merits.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 44, line 13. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 2 and 4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The scope of claims 2 and 4 is broader than the base claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 7-11, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or an antigen-binding fragment thereof that binds to binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 and not to non-neoplastic cells, the antibody or antigen binding fragment comprising the amino acid sequences of SEQ ID NOs:1 and 2 cells is not enabling for a protein comprising a polypeptide, which comprises a molecular chain of amino acids, wherein the polypeptide does not bind to the recited cells in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a purified polypeptide comprising an antibody, or a fragment thereof, that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and not to non-neoplastic cells, wherein the neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:1, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:3, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:1 or SEQ ID NO:3, wherein the purified peptide is a functional fragment comprising a fragment of the sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein the polypeptide is a functional

fragment selected from the group consisting of V_L, V_H, F_V, F_C, Fab, Fab', and $F(ab')_2$. The claims are further drawn to a purified polypeptide comprising an antibody or functional fragment, thereof, wherein the polypeptide comprises the amino acid sequence of SEQ IDNO:1, a purified polypeptide comprising an antibody or functional fragment, thereof, wherein the polypeptide comprises the amino acid sequence of SEQ IDNO:3 and a purified polypeptide comprising an antibody or functional fragment, thereof, wherein the polypeptide comprises the amino acid sequence of SEQ IDNO:1 and 3.

The specification discloses an IgM antibody, CM-1, (page 41line 16) that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and not to non-neoplastic cells, the antibody comprising a heavy chain variable region consisting of the amino acid sequence of SEQ ID NO: page 41, line 16, and a light chain variable region consisting of SEQ ID NO:2.

Claim 1 has three structural elements, a polypeptide, an antibody, or a functional fragment thereof. The only structural element that binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells is an antibody. The claim does not indicate whether the recited "a functional fragment" binds to the same antigen that the recited "an antibody" binds to. Therefore, the limitation "a functional fragment thereof" is broadly interpreted to encompass any functional fragment, for example Fc portion of an antibody.

The polypeptide recited in claims 4, 7-10, 15, and 16 does not necessarily binds to the cells recited in claim 1 for the following reasons: According to the Online dictionary, downloaded on 12/20/2006, from URL>>>m-w.com/dictionary, "antibody" is a protein of high molecular weight that are produced normally by specialized B cells after stimulation by an antigen and act specifically against the antigen in an immune response, that are produced abnormally by some cancer cells, and that typically consist of four subunits including two heavy chains and two light chains -- called also immunoglobulin, and "polypeptide" is a molecular chain of amino acids.
The specification does not teach any other polypeptide structure other than an antibody that binds to the recited cells in claim 1. Since the polypeptide of claims 4, 7-10, 15, and 16 do not necessarily comprise the required antigen binding heavy and light chains of an antibody, the claimed polypeptide does not necessarily binds any antigen. In addition, claim 4 states that the polypeptide inhibits any cancer cell, instead of the recited cancer cells of the base claim. The specification does not teach any other cancer cells are being inhibited other than the recited cells of claim 1.

In addition the claims are drawn to polypeptides that only contain 1 heavy chain variable region or 1 light chain variable region. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the

antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al. (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that antibodies as defined by the claims which may contain less than the full complement of heavy and light chain variable regions, have the required binding function of inducing apoptosis. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Furthermore, claim 14 is drawn to a functional fragment selected from the group V_L, V_H, F_V, F_C, Fab, Fab', and $F(ab')_2$. It is unclear how V_L, V_H, and F_C fragments can induces apoptosis of a neoplastic cell. Therefore in view It is unlikely that antibodies as defined by the claims which may contain less than the full complement of heavy and light chain variable regions, have the required binding function of inducing apoptosis.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention. It is unlikely that antibodies as defined by the claims which may contain less than the full complement of heavy and light chain variable regions, have the required binding function of inducing apoptosis.

Claims 1, 2, 4, 7, 8, 12 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a purified polypeptide comprising an antibody that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and not to non-neoplastic cells, wherein the neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:1, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:3, wherein the purified peptide comprises a sequence that is substantially identical to the amino acid of SEQ ID NO:1 or SEQ ID NO:3, wherein the antibody is

human, wherein the polypeptide is a functional fragment selected from the group consisting of V_L, V_H, F_V, F_C, Fab, Fab', and $F(ab')_2$.

The specification discloses an IgM antibody, CM-1, (page 41line 16) that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and not to non-neoplastic cells comprising a heavy chain variable region consisting of the amino acid sequence of SEQ ID NO: page 41line 16, and a light chain variable region consisting of SEQ ID NO:2. The specification further discloses that "substantially identical " encompasses a polypeptide exhibiting 75% identity to a reference amino acid sequence (page 13, lines 23-24).

The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

The Federal Circuit has recently clarified that a molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted

the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Thus, the instant specification may provide an adequate written description of the genus of polypeptides, per Lilly by structurally describing a representative number of the genus of polypeptides that function as claimed or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe the genus of antibodies in a manner that satisfies either the Lilly or Enzo standards. There is no description of the antigen bound by the genus of antibodies. There are insufficient structural features common to all members of the genus of antibodies. The genus of antibodies encompass an antibody that has a heavy chain variable region or a light chain variable region that has 75% identity to the respective chains of CM-1. Furthermore, the genus includes any human antibody that functions as claimed. This encompasses a multitude of antibodies. There is virtually no structural similarity between the genus of antibodies

as defined in the specification. The only antibody described in the specification is CM-1. One species of antibody, does not sufficiently describe the genus of antibodies and does not meet the standard set forth in Lilly.

The instant specification may also provide an adequate written description of the genus of polypeptide antagonists if the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. The specification discloses only one species of antibody. Thus, the specification does not describe sufficient structural characteristics that correlate with the ability of the genus of antibodies to function as contemplated by the specification and for the reasons set forth above do not meet the standards set forth by Enzo.

Thus, the specification does not provide an adequate written description of the genus of genus of polypeptide antagonists of claims 1, 2, 4, 7, 8, 12 and 15 that is required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhou et al (U.S. Patent Application Publication 2003/0190687, published Oct 9, 2003, priority filing date May 2, 2000) as evidenced by Huang et al (Cancer Research 2001, 61:6918-6924).

The claims are drawn to a purified polypeptide comprising an antibody that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and not to non-neoplastic cells, wherein the neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell.

Zhou et al describe an antibody to TRAIL that binds to and induced apoptosis of neoplastic cells but not to non-neoplastic cells (paragraphs 0241- 0247).

As evidenced by Huang et al., TRAIL is expressed on the cell line HT-29 (page 6920, 1st column).

Summary

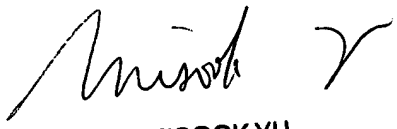
No claims allowed.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Halvorson, PhD
Patent Examiner
571-272-6539



MISOOK YU
PRIMARY EXAMINER